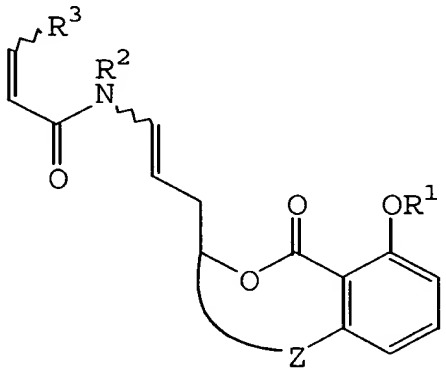
AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method of treating an intra-organellar acidification of intracellular organelles by the inhibition of vacuolar-type (H+)-ATPase, said method comprising administering to a patient an amount effective to treat intra-organellar acidification of intracellular organelles of a vacuolar-type (H+)-ATPase of at least one compound of the formula:



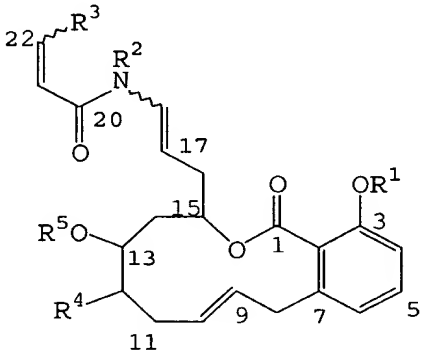
(I),

wherein R^1 and R^2 are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R^6CH_2-, R^6CO-, or R^6SO_2-, wherein R^6 is H, a straight-chain or branched saturated or unsaturated alkyl, or an aryl; R^3 is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; the aromatic ring is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; the saturated alkyl, unsaturated alkyl and aryl substituents defined in R^1-R^3 and R^6 are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and Z is a contiguous linker comprising a chain of 7-10 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship with OR^1 and ending with the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 12-15 membered ring; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof~~,~~.

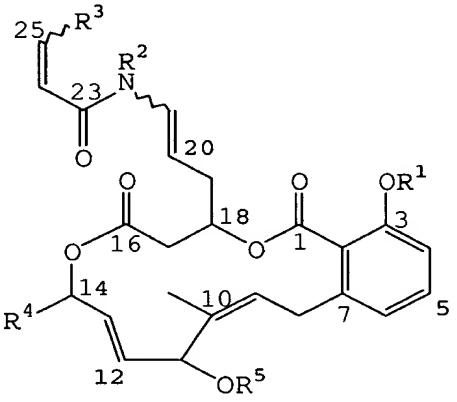
2. (Previously Presented) The method of claim 1, wherein Z is a contiguous linker comprising a chain of 7-10 atoms which, together with the five atoms beginning with the carbon of the aromatic ring of formula (I) in meta-relationship with OR^1 and ending with

the carbon directly attached to the alkyl oxygen of the lactone of formula (I), said carbons being covalently bonded to either end of linker Z, integrally form a 12-15 membered ring.

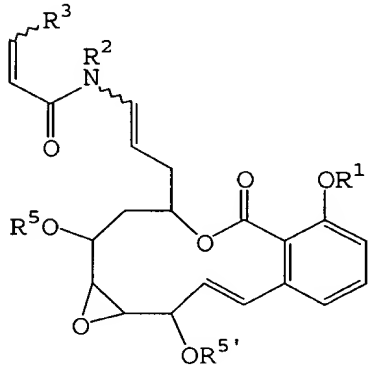
3. (Previously Presented) The method of claim 1, wherein said compound is selected from the group consisting of:



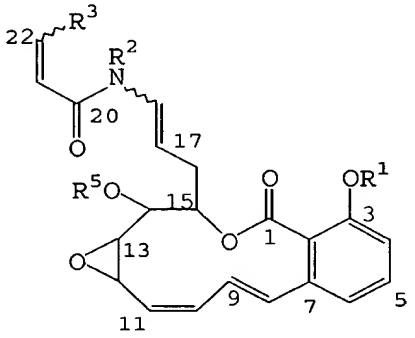
(IA),



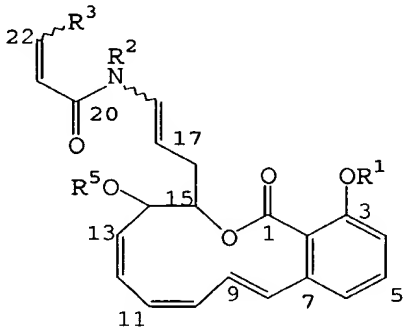
(IB),



(IC),



(ID),

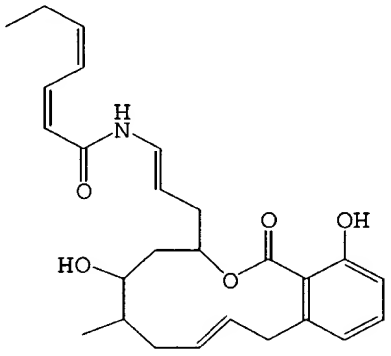


and (IE),

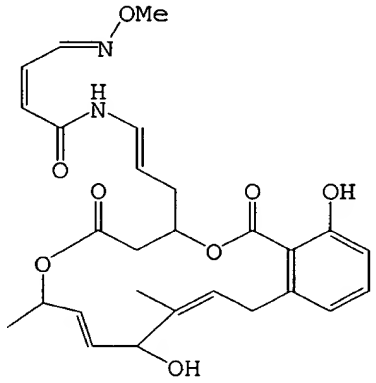
wherein R^1 and R^2 are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, R^6CH_2-, R^6CO-, or R^6SO_2-, wherein R^6 is H, a

straight-chain or branched saturated or unsaturated alkyl, or an aryl; R^3 is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, an oxime, or an oxime methyl ether; R^4 is H, an alkyl, or R^7CH_2-, wherein R^7 is R^6O-, R^6CO_2-, or R^6SO_3-; R^5 and $R^{5'}$ are the same or different and each is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, R^6CH_2-, R^6CO-, or R^6SO_2-; the saturated alkyl, unsaturated alkyl and aryl defined in R^1-R^3, R^5, $R^{5'}$ and R^6, and the alkyl defined in R^4, are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; and the aromatic ring of formula (I) is unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

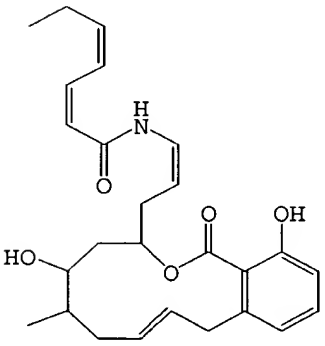
4. (Previously Presented) The method of claim 3, wherein said compound is selected from the group consisting of:



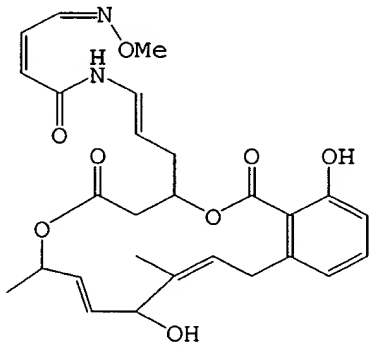
salicylihalamide A,



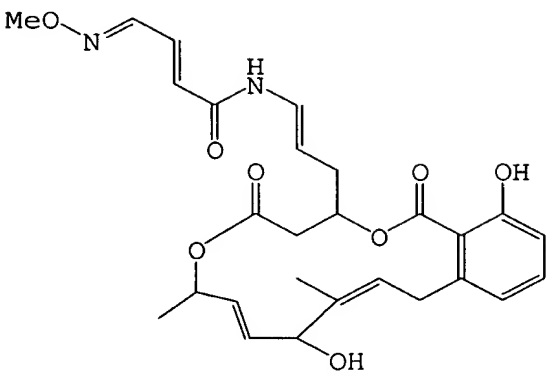
lobatamide A,



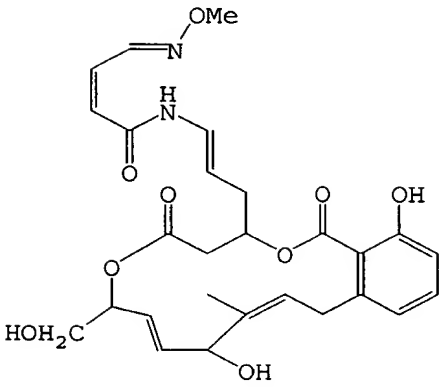
salicylihalamide B,



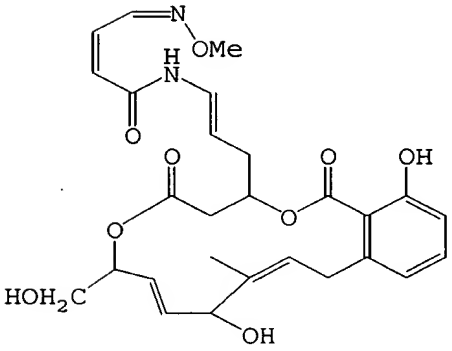
lobatamide B,



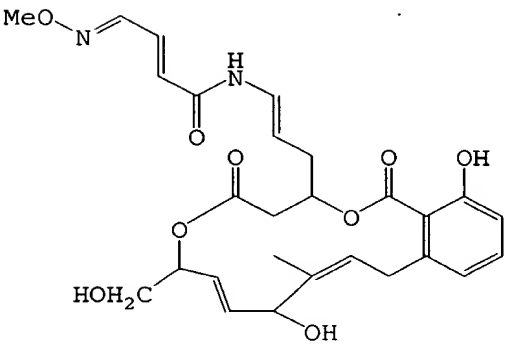
lobatamide C,



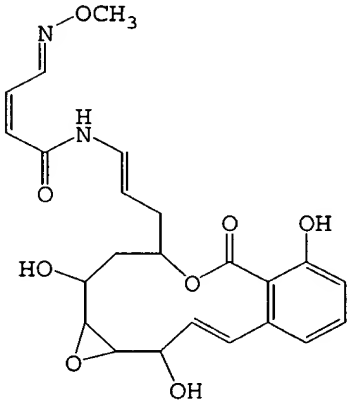
lobatamide D,



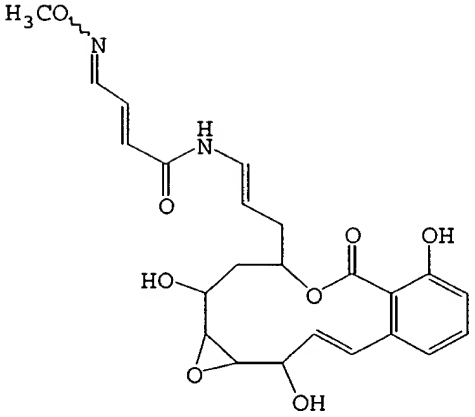
lobatamide E,



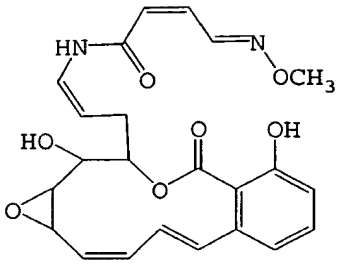
lobatamide F,



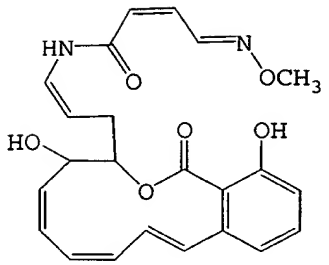
CJ-12,950,



CJ-13,357,



oximidine 1, and

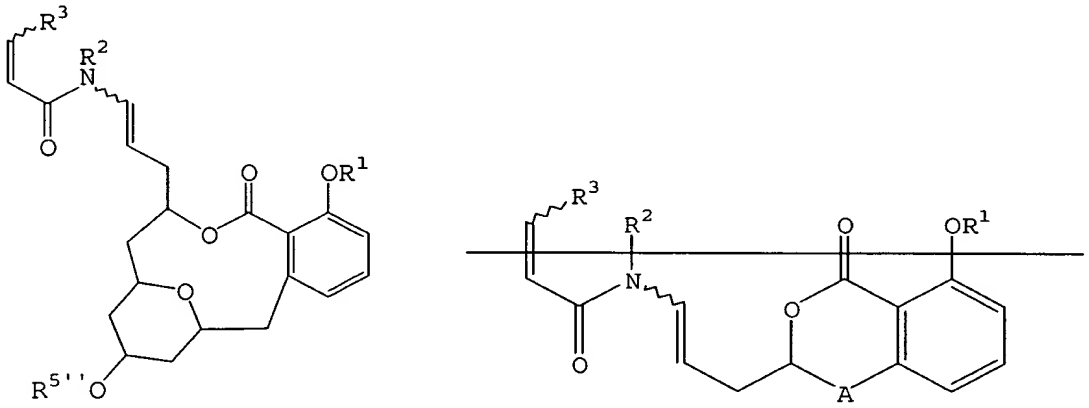


oximidine 2;

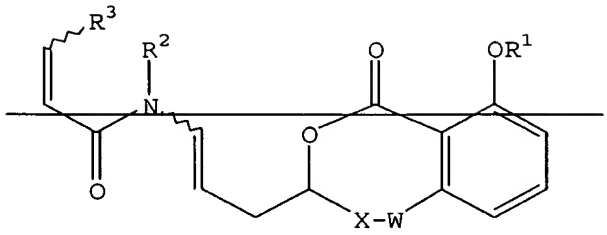
or a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

5. (Previously Presented) The method of claim 1, wherein Z is a contiguous linker comprising a chain of 7-10 atoms which, together with the five atoms beginning with the carbon of the aromatic ring in meta-relationship with OR^1 and ending with the carbon directly attached to the alkyl oxygen of the lactone, said carbons being covalently bonded to either end of linker Z, integrally form a 12-15 membered ring.

6. (Currently Amended) A method of treating an intra-organellar acidification of intracellular organelles by the inhibition of vacuolar-type (H+)-ATPase, said method comprising administering to a patient an amount effective to treat intra-organellar acidification of intracellular organelles of a vacuolar-type (H+)-ATPase of at least one compound of the formula:



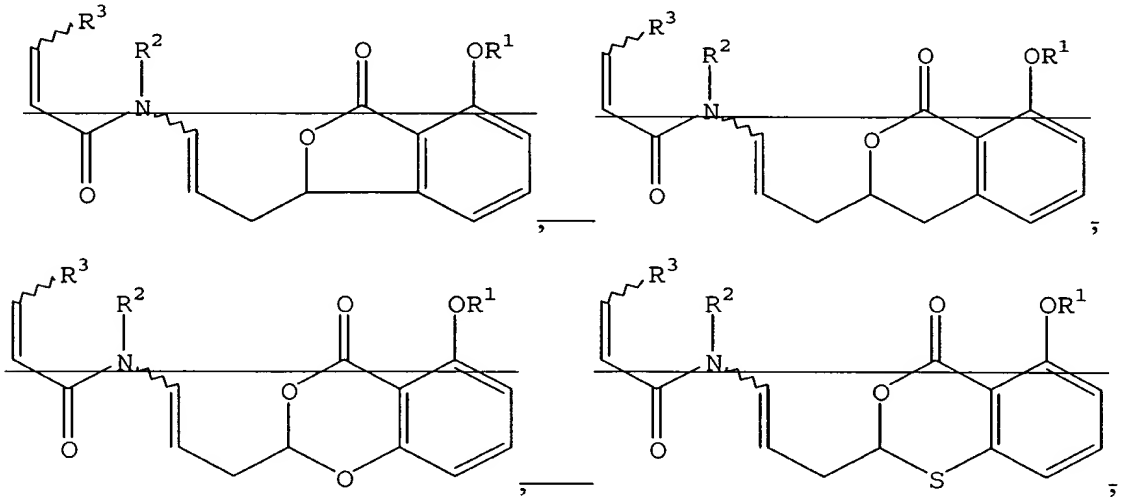
(IF); ~~(IG)~~

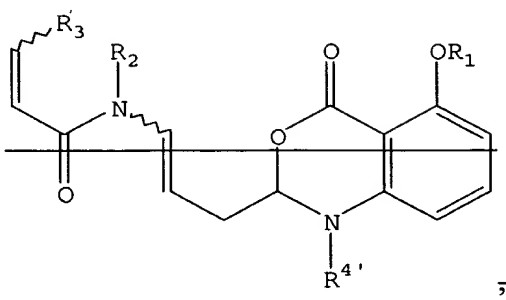


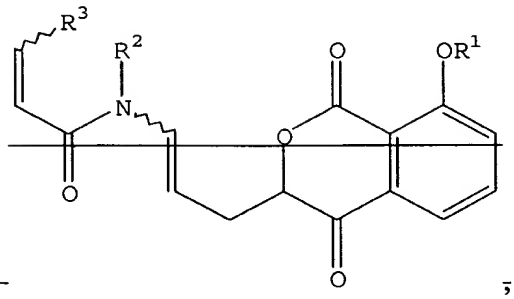
~~and (III),~~

wherein R^1-R^3 are as defined in claim 1; and $R^{5''}$ is H, a straight-chain or branched saturated or unsaturated alkyl, an aryl, a glycoside, R^6CH_2-, R^6CO-, or R^6SO_2-, wherein R^6 is as defined in claim 1; and the saturated alkyl, unsaturated alkyl and aryl defined in $R^{5''}$ are unsubstituted or substituted with at least one substituent selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano~~; A is a covalent bond or a C_1-C_6 straight-chain saturated or unsaturated alkyl linker which is unsubstituted or is substituted with a one or more substituents selected from the group consisting of a halogen, a nitro, an amino, a hydroxyl, a thio, an acyl, an alkyl, and a cyano; X is a covalent bond or a C_1-C_5 straight-chain saturated or unsaturated alkyl linker which is unsubstituted or is substituted with a one or more substituents selected from the group consisting of a halogen, a nitro, an amino, hydroxyl, thio, acyl, C_1-C_6 alkyl, and cyano; and W is O, S, C(O), C(S), $S(O)_n$ or N-$R^{4'}$, wherein $R^{4'}$ is H, C_1-C_6 straight-chain or branched saturated or unsaturated alkyl, aryl, R^6CH_2-, R^6CO-, or R^6SO_2-, R^6 is as defined in claim 1, and n is an integer from 0-2~~.

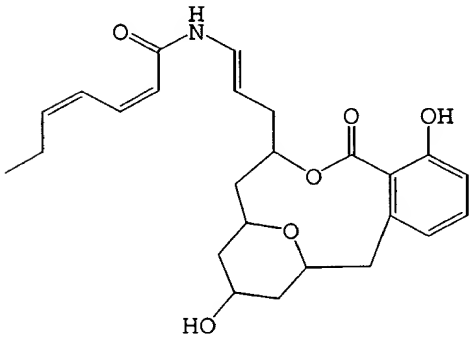
7. (Currently Amended) The method of claim 6, wherein said compound is selected from the group consisting of:

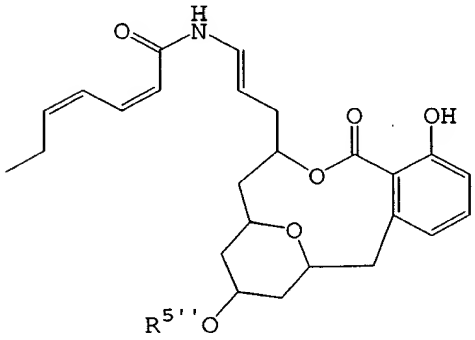






~~, and~~





apicularen A and apicularen B,

wherein $R^{5''}$ is N-acetyl-β-D-glucosamine.

8. (Previously Presented) The method of claim 1, which further comprises co-administering to a patient in need thereof a therapeutically effective amount of at least one additional compound other than a compound defined in claim 1.

9. (Previously Presented) The method of claim 8, wherein said additional compound is selected from the group consisting of bafilomycins and concanamycins.

10. (Previously Presented) The method of claim 9, wherein said additional compound is concanamycin A.

11. (Previously Presented) The method of claim 9, wherein said additional compound is bafilomycin A_1.

12. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H+)-ATPase inhibiting-effective amount is effective to inhibit intra-organellar acidification of intracellular organelles.

13. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H+)-ATPase inhibiting-effective amount is effective to inhibit urinary acidification.

14. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H+)-ATPase inhibiting-effective amount is effective to inhibit bone resorption.

15. (Previously Presented) The method of claim 14, wherein said vacuolar-type (H+)-ATPase inhibiting-effective amount is effective to treat osteoporosis.

16. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H+)-ATPase inhibiting-effective amount is effective to inhibit fertility.

17. (Previously Presented) The method of claim 1, wherein said vacuolar-type (H+)-ATPase inhibiting-effective amount is effective to inhibit angiogenesis.

Claims 18-31 (Canceled)